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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>7</sup> : C12N 15/00, A01K 67/027, C07K 14/81, C12N 5/06</p> <p>(21) International Application Number: PCT/US99/25786</p> <p>(22) International Filing Date: 2 November 1999 (02.11.99)</p> <p>(30) Priority Data: Not furnished 2 November 1998 (02.11.98) US 60/131,061 26 April 1999 (26.04.99) US 60/131,328 26 April 1999 (26.04.99) US 60/149,317 17 August 1999 (17.08.99) US</p> <p>(71) Applicant (for all designated States except US): TRUSTEES OF TUFTS COLLEGE [US/US]; Medford, MA 02155 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): BAGUISI, Alexander, B. [PH/US]; Nine Millbury Street, Grafton, MA 01519 (US). OVERSTROM, Eric, W. [US/US]; 32 Blanchard Road, Grafton, MA 01519 (US).</p> <p>(74) Agents: PIERCE, N., Scott et al.; Hamilton, Brook, Smith &amp; Reynolds, P.C., Two Militia Drive, Lexington, MA 02421 (US).</p>	<p>A3</p>	<p>(11) International Publication Number: WO 00/25578</p> <p>(43) International Publication Date: 11 May 2000 (11.05.00)</p> <p>(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p><b>Published</b> <i>With international search report.</i></p> <p>(88) Date of publication of the international search report: 16 November 2000 (16.11.00)</p>
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(54) Title: METHODS FOR CLONING ANIMALS

(57) Abstract

The present invention pertains to methods for cloning animals. In particular, the invention includes methods of cloning an animal by combining a genome from an activated donor cell with an activated enucleated oocyte to thereby obtain a nuclear transfer embryo, and impregnating an animal with the nuclear transfer embryo in conditions suitable for gestation of a cloned animal. The invention further relates to methods of chemically enucleating an oocyte having a meiotic spindle apparatus by exposing the oocyte with a compound that destabilizes the meiotic spindle apparatus.

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**INTERNATIONAL SEARCH REPORT**

International Application No	
PCT/US 99/25786	

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>				
IPC 7	C12N15/00	A01K67/027	C07K14/81	C12N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K A01K C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 01163 A (UNIV MASSACHUSETTS) 14 January 1999 (1999-01-14)  page 11, line 23 -page 12, line 21 page 16, line 20 -page 19, line 7; claims 1-13,15-22  ---	1-5,7-9, 11-17, 19-26, 28-30
A	CIBELLI J B ET AL: "CLONED TRANSGENIC CALVES PRODUCED FROM NONQUIESCENT FETAL FIBROBLASTS" SCIENCE,US,AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, vol. 280, 22 May 1998 (1998-05-22), pages 1256-1258, XP000786003 ISSN: 0036-8075 the whole document  ---	1-5,7  -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
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Date of the actual completion of the international search

24 August 2000

Date of mailing of the international search report

31.08.00

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

Intern	nal Application No
PCT/US 99/25786	

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ROBL J M ET AL: "SOMATIC CELL NUCLEAR TRANSPLANTATION IN CATTLE" ANNUAL MEETING SOC. STUDY REPROD., vol. 58, 8 August 1998 (1998-08-08), page 25 XP000791151 the whole document ---	1
A	WO 96 26268 A (GENZYME TRANSGENICS CORP) 29 August 1996 (1996-08-29) the whole document ---	1
P,X	BAGUISI A, ET AL.: "Production of goats by somatic cell nuclear transfer." NAT BIOTECHNOL, vol. 17, no. 5, May 1999 (1999-05), pages 456-461, XP000891364 page 457, column 1, paragraph 2 page 459, column 1, paragraph 3 -column 2, paragraph 4 page 460, column 1, paragraph 2 page 460, column 2, paragraph 1 ---	1-4, 6-19, 21-30
A	BORDIGNON V ET AL: "TELOPHASE ENUCLEATION: AN IMPROVED METHOD TO PREPARE RECIPIENT CYTOPLASTS FOR USE IN BOVINE NUCLEAR TRANSFER" MOLECULAR REPRODUCTION AND DEVELOPMENT,US, NEW YORK, NY, vol. 49, January 1998 (1998-01), pages 29-36, XP000910821 cited in the application the whole document ---	31
A	WO 98 29532 A (PEURA TEIJA ;UNIV MONASH (AU)) 9 July 1998 (1998-07-09) the whole document ---	31
A	WO 95 03398 A (UNIV MONASH ;TATHAM BRENDAN GEORGE (AU)) 2 February 1995 (1995-02-02) the whole document ---	31
P,A	US 5 952 222 A (ROSENKRANS JR CHARLES F ET AL) 14 September 1999 (1999-09-14) the whole document -----	31

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 99/25786

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  

As far as claims 8 to 30 are directed to a method of treatment of the non human animal body, the search has been carried out and based on the alleged effects of the composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

**1. Claims: 1-30**

Methods for cloning an animal or producing a transgenic animal comprising the steps of:  
a) combining a genome from an activated donor cell with an activated, enucleated oocyte to thereby form a nuclear transfer embryo; and;  
b) impregnating an animal with the nuclear transfer embryo in conditions suitable for gestation of the cloned animal.

**2. Claims: 31-38**

A method of enucleating an oocyte having a meiotic spindle apparatus, comprising exposing the oocyte with at least one compound that destabilizes the meiotic spindle apparatus;

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 99/25786

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
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